

In the Claims

Please cancel claims 8, 21-45, 67-79, and 81-82, without prejudice to their presentation in a continuing patent application. Please amend claims 1-7, 8-20, 46-66, 80 and 83 as follows:

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1. (Amended) A [pharmaceutical] composition comprising at least one oligonucleotide in an emulsion and a penetration enhancer.
 2. (Amended) The [pharmaceutical] composition of claim 1 wherein said oligonucleotide is an antisense oligonucleotide.
 3. (Amended) The [pharmaceutical] composition of claim 1 wherein said oligonucleotide modulates expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses.
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 4. (Amended) The [pharmaceutical] of claim 1 wherein said oligonucleotide is selected from the group consisting of a ribozyme, a peptide nucleic acid, a molecular decoy, an external guide sequence [or] and an aptamer.

5. (Amended) The [pharmaceutical] composition of claim 1 wherein said emulsion is selected from the group consisting of an oil-in-water emulsion, a water-in-oil emulsion, an oil-in-water-in-oil emulsion [or] and a water-in-oil-in-water emulsion.

6. (Amended) The [pharmaceutical] composition of claim 1 wherein said emulsion is a microemulsion.

7. (Amended) The [pharmaceutical] composition of claim 6 wherein said microemulsion is selected from the group consisting of an oil-in-water microemulsion, a water-in-oil microemulsion, an oil-in-water-in-oil microemulsion [or] a water-in-oil-in-water microemulsion.

9. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is a fatty acid.

10. (Amended) The [pharmaceutical] composition of claim 9 wherein said fatty acid is selected from a group consisting of arachidonic acid, oleic acid, lauric acid, caprylic acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprinate, tricaprinate, monoolein, dilaurin, glyceryl 1-monocaprinate, 1-dodecylazacycloheptan-2-one, an acylcarnitine, an acylcholine, [or] a monoglyceride, a diglyceride [or] and a pharmaceutically acceptable salt thereof.

11. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is a bile salt.

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12. (Amended) The [pharmaceutical] composition of claim 11 wherein said bile salt is selected from [a] the group consisting of cholic acid, dehydrocholic acid, deoxycholic acid, glucolic acid, glycholic acid, glycodeoxycholic acid, taurocholic acid, taurodeoxycholic acid, chenodeoxycholic acid, ursodeoxycholic acid, sodium tauro-24,25-dihydro-fusidate, sodium glycodihydrofusidate, polyoxyethylene-9-lauryl ether [or] and a pharmaceutically acceptable salt thereof.

13. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is a combination of at least one fatty acid and at least one bile salt.

14. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is a chelating agent.

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15. (Amended) The [pharmaceutical] composition of claim 14 wherein said chelating agent is selected from [a] the group consisting of EDTA, citric acid, a salicylate, [a] an *N*-acyl derivative of collagen, laureth-9, an *N*-amino acyl derivative of a beta-diketone [or] and a mixture thereof.

16. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is a surfactant.

17. (Amended) The [pharmaceutical] composition of claim 16 wherein said surfactant is selected from [a] the group consisting of sodium lauryl sulfate, polyoxyethylene-9-lauryl ether, polyoxyethylene-20-cetyl ether, a perfluorchemical emulsion [or] and a mixture thereof.

18. (Amended) The [pharmaceutical] composition of claim 8 wherein said penetration enhancer is selected from [a] the group consisting of unsaturated cyclic ureas, 1-alkyl-alkanones, 1-alkenylazacyclo-alkanones, steroidal anti-inflammatory agents and mixtures thereof.

19. (Amended) The [pharmaceutical] composition of claim 1 further comprising at least one carrier compound.

20. (Amended) The [pharmaceutical] composition of claim 19 wherein said carrier compound is selected from [a] the group consisting of polyinosinic acid, dextran sulfate, polycytidic acid, lipofectin, cationic glycerol derivatives, polylysine and 4-acetamido-4'isothiocyano-stilbene-2,2'-disulfonic acid.

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46. (Amended) A [pharmaceutical] composition comprising an oligonucleotide in oral dosage form.

47. (Amended) The [pharmaceutical] composition of claim 46 wherein [at least one of said covalent linkages of] said oligonucleotide comprises at least one [is a] modified covalent linkage.

sub 11

48. (Amended) The [pharmaceutical] composition of claim 47 wherein said modified covalent linkage is selected from the group consisting of a phosphorothioate linkage, a phosphotriester linkage, a methyl phosphonate linkage, a methylene(methylimino) linkage, a morpholino linkage, an amide linkage, a polyamide linkage, a short chain alkyl intersugar linkage, a cycloalkyl intersugar linkage, a short chain heteroatomic intersugar linkage and a heterocyclic intersugar linkage.

49. (Amended) The [pharmaceutical] composition of claim 46 wherein [at least one of the nucleotides of] said oligonucleotide comprises at least one [has a] modified sugar moiety.

50. (Amended) The [pharmaceutical] composition of claim 49 wherein said modified sugar moiety has a substitution or addition at the 2' position of a moiety selected from the group consisting of -OH, -SH, -SCH₃, -F, -OCN, -OCH₃OCH₃, -OCH₃O(CH₂)_nCH₃, -

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O(CH₂)_nNH₂ or -O(CH₂)_nCH₃ where n is from 1 to about 10, a C₁ to C₁₀ lower alkyl group, an alkoxyalkoxy group, a substituted lower alkyl group, a substituted alkaryl group, a substituted aralkyl group, -Cl, -Br, -CN, -CF₃, -OCF₃, an -O-alkyl group, an -S-alkyl group, an N-alkyl group, an O-alkenyl group, an S-alkenyl group, an N-alkenyl group, -SOCH₃, -SO₂CH₃, -ONO₂, -NO₂, -N₃, -NH₂, a heterocycloalkyl group, a heterocycloalkaryl group, an aminoalkylamino group, a polyalkylamino group, a substituted silyl group, an RNA cleaving group, a reporter group, a DNA intercalating group, a group for improving the pharmacokinetic properties of an oligonucleotide, a group for improving the pharmacodynamic properties of an oligonucleotide, a methoxyethoxy group and a methoxy group.

51. (Amended) The [pharmaceutical] composition of claim 46 wherein [at least one of the nucleotides of] said oligonucleotide comprises at least one [has a] modified nucleobase.

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52. (Amended) The [pharmaceutical] composition of claim 46 wherein said oral dosage form is selected from the group consisting of tablets, capsules and gel capsules.

53. (Amended) The [pharmaceutical] composition of claim 46 wherein said oligonucleotide is an antisense oligonucleotide.

54. (Amended) The [pharmaceutical] composition of claim 46 wherein said oligonucleotide modulates expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses.

55. (Amended) The [pharmaceutical] composition of claim 46 wherein said nucleic acid is a ribozyme, a peptide nucleic acid, an external guide sequence, a molecular decoy or an aptamer.

56. (Amended) The [pharmaceutical] composition of claim 46 further comprising an enteric material that substantially prevents dissolution of said tablets, capsules or gel capsules in a mammalian stomach.

57. (Amended) The [pharmaceutical] composition of claim 56 wherein said enteric material is a coating.

58. (Amended) The [pharmaceutical] composition of claim 57 wherein said enteric coating is selected from the group consisting of acetate phthalate, propylene glycol, sorbitan monoleate, cellulose acetate trimellitate, hydroxy propyl methyl cellulose phthalate [or] cellulose acetate phthalate.

59. (Amended) The [pharmaceutical] composition of claim 46 further comprising a penetration enhancer.

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60. (Amended) The [pharmaceutical] composition of claim 59 wherein said penetration enhancer is selected from the group consisting of bile salts and fatty acids.

61. (Amended) The [pharmaceutical] composition of claim 60 wherein said bile salt is selected from the group consisting of ursodeoxycholic acid, chenodeoxycholic acid, and salts thereof.

62. (Amended) The [pharmaceutical] composition of claim 60 wherein said fatty acids are selected from the group consisting of capric acid, lauric acid, and salts thereof.

63. (Amended) The [pharmaceutical] composition of claim 46 further comprising an excipient.

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64. (Amended) The [pharmaceutical] composition of claim 63 wherein said excipient is selected from the group consisting of polyethyleneglycol and precirol.

65. (Amended) The [pharmaceutical] composition of claim 46 further comprising a plasticizer.